

# Visudyne helpful for rubeosis iridis

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in Heidelberg

PHOTODYNAMIC therapy (PDT) with the photosensitizer verteporfin (Visudyne, QLT/Novartis) can successfully treat both rubeosis iridis and neovascular glaucoma, but the effects are short lived, reported Valeska Müller MD, Berlin Eye Day Hospital in Berlin, Germany at the 20th Congress of the DGII (Deutschsprachige Gesellschaft für Intraokularlinsen Implantation und refraktive Chirurgie).

"Rubeosis iridis is treatable with PDT in combination with verteporfin, causing vascular occlusion without damaging any physiologic tissues. The occlusion of neovascular vessels is directly dependent on the dose of light applied. Unfortunately, however, the duration of the therapeutic effect following treatment is limited. This technique is plausible in patients with neovascular glaucoma or in those patients with rubeosis iridis who must undergo cataract surgery," she said.

Dr Müller discussed the results of a new single-centre, prospective, open-label, phase II, intra-individual, controlled, pilot, dose-finding study designed to establish

the treatment parameters for PDT with verteporfin in this patient group. She treated nine patients with Visudyne who had rubeosis iridis due to proliferative diabetic vitreo-retinopathy (PDVR), central retinal vein occlusion (CRVO) or carotid artery stenosis.

All patients received panretinal laser treatment of at least 1,500 spots at least six weeks before PDT, and still presented with rubeosis. Two of the patients had neovascular glaucoma (NVG) at baseline. She noted that Visudyne therapy was effective in patients who did not benefit from panretinal laser photocoagulation.

The treatment involved subdividing the iris into four quadrants and treating two opposing quadrants in one single sitting, with two different energy levels per patient group. She divided the patients into three separate groups according to the energy level to be applied. The other two iris quadrants represented intra-individual controls that received only drug treatment.

Following the application of verteporfin, Dr Müller administered laser at 600mW/cm<sup>2</sup> for 15 minutes following the start of infusion. The applied energy doses varied between 15 J/cm<sup>2</sup> and 100 J/cm<sup>2</sup> at a fluence rate of 600mW.

Dr Müller recorded data at baseline and at one, four and 12 weeks following therapy. She defined the primary effects of treatment as the changes in the hyperfluorescence seen in iris angiography, as compared to the data recorded at baseline.

She observed a significant hyperfluorescence after PDT therapy in six patients who were radiated with 75 J/cm<sup>2</sup>, and in three patients who were radiated with 100 J/cm<sup>2</sup>, as shown by the iris angiographic data taken at one and four weeks.

Other study criteria showed

no significant changes in the pre- and post-PDT data, including visual acuity, intraocular pressure (12-28mmHg), posterior chamber flare (~35 pc/s) and iris/stroma structure. Dr Müller explained that although vision was not improved by this treatment, the point of therapy was to prevent and eventually treat NVG.

## Repeat treatments necessary

Mike Holzer MD, Heidelberg University Eye Clinic, Heidelberg, Germany, used PDT against corneal neovascularisation in an experimental study he conducted in 2003. He commented that although PDT can be used for neovascular glaucoma and corneal neovascularisation, his own experience with this treatment modality showed that it had to be repeated once there was vascular regrowth and that the treatment was only helpful in certain phases of neovascularisation.

As long as there is a stimulus for vascular regrowth, neovascularisation will recur. The therapy can be effective for days or weeks, but unfortunately will need to be repeated, he said.

Dr Holzer confirmed Dr Müller's observation that PDT was not damaging to the surrounding tissues, i.e. the cornea and iris in his studies, and that the therapy was a good option for the temporary occlusion of any kind of neovascularisation.

According to Dr Müller, the results of Visudyne therapy for rubeosis iridis were very promising. PDT could be a useful adjuvant instrument for eye surgeons to stop the progression of rubeosis iridis as well as to avoid the onset of neovascular glaucoma, she said. She cautioned, however, that the fourth- and twelfth-week controls demonstrated a temporary duration of treatment and that recanalisation and re-treatment were inevitable.

She noted that since neovascularisation starts at the pupillary margin in approximately 95% of cases and reaches toward the chamber angle, her goal was to occlude those vessels in order to prevent further progression. Furthermore, she observed that since the laser has a certain tissue penetration depth at the wavelengths employed, this method could prove effective in directly radiating areas of neovascularisation around the chamber angle (without a gonioscope) in cases of open angle glaucoma causing occlusion and regression.

She said that CRVO cases require several weeks following panretinal laser treatment for regression to occur. During this critical time period, vessel growth stimulus from the retina can lead to NVG in some cases. Occluding these vessels straight away in these patients might fill

the time gap until retinal laser treatment itself leads to regression, she said.

## Standard therapies frequently ineffective

Dr Müller noted that current therapies for proliferative retinopathies with rubeosis iridis included panretinal laser photocoagulation, cyclocryotherapy and pars plana vitrectomy. With these methods, a regression from rubeosis can be observed in a maximum of 60%-80% of patients, after a therapeutic window of four to six weeks, she explained. This means that there are approximately 20% of patients who are classified as "non-responders" to panretinal photocoagulation and for whom alternative solutions are required.

She said that neovascular glaucoma was a much-feared complication in ischemic retinopathy, frequently leading to blindness or enucleation. To date, there is no satisfactory therapy concerning this serious condition, she emphasised.

The main causative factors of neovascular glaucoma are the ischemic type of central retinal vein occlusion in which 40% of patients develop neovascular glaucoma, proliferative diabetic vitreoretinopathy in which 32%-64% of patients develop neovascular glaucoma and carotid stenosis in which 12% of cases develop neovascular glaucoma.

Dr Müller explained that once injected, verteporfin builds a complex with the LDLs of the vessel walls. The dye accumulates in this fashion on the endothelium of neovascular tissues. Verteporfin can then be activated through laser light (689nm) thus producing free radicals. These free radicals cause damage to the vascular endothelium and subsequently occlude neovascularisations. Dr Müller emphasised that neighbouring tissues remained unharmed through this process.

Dr Müller confirmed a complete regression of rubeosis after approximately 15 weeks post PDT in two of the study patients. She noted that in light of the latest results in anti-VEGF therapy studies, combination treatment with PDT and anti-VEGF drugs could certainly be very useful in these cases.

As patients only received treatment within the framework of the investigation, Dr Müller was not able to comment on retreatments in this study group.

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